

Appl. No. 10/719,196  
Amdt. dated September 13, 2006  
Reply to Office Action mailed October 28, 2005

### **REMARKS/ARGUMENTS**

Claims 18, 21-34 and 54 are pending. Claims 1-17, 19, 20 and 35-53 have been cancelled without intending to abandon or to dedicate to the public any patentable subject matter. As set forth more fully below, reconsideration and withdrawal of the Examiner's rejections of the claims are respectfully requested.

#### **Rejections Under 35 U.S.C. § 112, Second Paragraph**

The Examiner has rejected Claims 18, 20-26, 29-31 and 32 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Specifically, the Examiner notes that the claims recite an enzyme having farnesyl phosphate as a substrate whereas the specification provides support for a phosphatase acting on farnesyl pyrophosphate. Applicants have amended Claim 18 to recite a phosphatase enzyme that acts on farnesyl pyrophosphate. Applicants therefore submit that the recitation of the phosphatase enzyme is sufficiently definite to meet the requirements of 35 U.S.C. § 112, second paragraph.

#### **Rejections Under 35 U.S.C. § 112, First Paragraph**

The Examiner has rejected Claims 18, 20-31, 33 and 34 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention and as lacking enablement for using any microorganism in the methods of the invention other than those shown in the Examples section of the specification. Specifically, the Examiner states that the claims are generic for any microorganism 1) having reduced squalene synthase activity or 2) that is an erg<sup>9</sup> mutant.

In fact, the pending claims require a microorganism that:

- 1) can be cultured in a fermentation medium,
  - 2) have an isoprenoid metabolic pathway having a squalene synthase gene,
  - 3) have at least one gene for a phosphatase having farnesyl pyrophosphate as a substrate,
  - 4) has been genetically modified to decrease the action of the squalene synthase gene,
- and 5) has been genetically modified to increase the action of the phosphatase having farnesyl pyrophosphate as a substrate.

The subset of microorganisms falling within this limiting definition cannot be described as “any microorganism existing in nature” as stated by the Examiner.

Similarly, in the Examiner’s analysis of the ‘Wands’ factors’ for determining if undue experimentation is necessary to carry out the methods of the invention, the Examiner states that the claimed methods encompass the use of “any microorganism existing in nature and engineered, wherein the action of squalene synthase is reduced.” Using this definition, the Examiner argues that the pending claims are too broad to be supported by the specific Examples provided in the specification. Applicants submit that this definition misstates, or significantly understates, the limitations imposed on the currently claimed microorganisms. The subset of microorganisms meeting the five limitations listed above is narrower than “any microorganism existing in nature.”

Additionally, the Examiner notes that the specific examples provided in the specification describe the use of *S. cerevisiae* and *E. coli*. and argues, therefore, that the direction or guidance presented in the specification is insufficient to support the use of any microorganism in the claimed methods, and that one of skill in the art would be required to undertake undue experimentation to mutate all known microorganisms, with any chemical mutagen, followed by the screening of all mutants for those having reduced or absent squalene synthase activity. It is the Examiner’s position that while the required methods are well known and the skills of those of the relevant art are high, the skilled artisan could only carry out the claimed methods with the two microorganisms for which specific examples are provided. But Applicants submit that undue

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experimentation is not viewed solely in light of the examples provided. Indeed, as stated in the guidance provided by section 2164.02 of the MPEP:

The presence of only one working example should never be the sole reason for rejecting claims as being broader than the enabling disclosure, even though it is a factor to be considered along with all the other factors. To make a valid rejection, one must evaluate all the facts and evidence and state why one would not expect to be able to extrapolate that one example across the entire scope of the claims.

In this instance, the Examiner is arguing that the reason the highly skilled artisan could not use the well known methods to extrapolate the working examples provided to the entire scope of the claims is that it would involve too much work. But this is distinct from too much experimentation. As the Examiner notes, the methodology used to arrive at the organisms is well known, and the relevant skill in the art is high, and, as Applicants have described above, the subset of claimed microorganisms is relatively narrow. Thus, there is little experimentation necessary for one of skill in the art to carry out the known methods necessary to practice the presently claimed invention. However, Applicants agree with the Examiner that these known methods are labor intensive and require the skilled artisan to perform laboratory work to practice the invention. But this labor, and the work necessary, are not experimentation with an unknown outcome - they are merely the application of known methods by skilled artisans in which the outcome has been shown by working examples in the instant specification. Thus, the Examiner's review of the 'Wands' factors' confuses a labor intensive method with undue experimentation to conclude that the currently claimed methods are not enabled by the present specification. Applicants submit that too much work is not to be equated with undue experimentation and that the working examples and accompanying description provide adequate enablement for the currently claimed methods.

In view of the foregoing remarks, applicants submit that there is adequate enablement in the specification for Claims 18 and 21-34, as amended, and request the Examiner's rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

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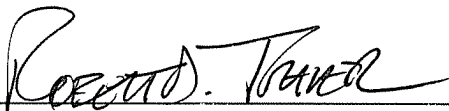
Double Patenting

The Examiner has rejected Claim 24 under 35 U.S.C. § 101 as claiming the same invention as that of Claim 24 of U.S. Patent No. 6,689,593. Applicants have amended Claim 24 to remove material that overlaps the methodology of Claim 24 of U.S. Patent No. 6,689,593. In light of these amendments to the currently pending Claim 24, Applicants believe that this double patenting rejection under 35 U.S.C. § 101 is moot.

Based upon the foregoing, Applicants believe that all pending claims are in condition for allowance and such disposition is respectfully requested. In the event that a telephone conversation would further prosecution and/or expedite allowance, the Examiner is invited to contact the undersigned.

Respectfully submitted,

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